Amendments to the Specification

Please replace the paragraph bridging pages 5 and 6 of the specification with the following new paragraph:

Membrane proteins generally have three distinct segments: the extracellular domain, the transmembrane domain, and the intracellular domain. The extracellular domain is the part of the protein that sticks out of the membrane on the outside of the cell or the luminal face of an intracellular organelle. If the polypeptide chain of the protein crosses the bilayer several times, the extracellular domain can comprise several "loops" sticking out of the membrane. This domain can facilitate the binding of ligands. The transmembrane domain spans the membrane. In the majority of proteins for which structural evidence exists, transmembrane alpha helices make up most of the transmembrane domain. In certain proteins, such as the nicotinic acetylcholine receptor, the transmembrane domain forms a protein-lined pore through the membrane, or ion channel. Upon activation of an extracellular domain by binding of the appropriate ligand, the pore becomes accessible to ions, which then pass through. In other proteins, the transmembrane domains are presumed to undergo a conformational change upon binding, which exerts an effect intracellular1y. In some receptors, such as members of the 7TM superfamily (e.g. GPCRs), the transmembrane domain may contain the ligand binding pocket (evidence for this and for much of what else is known about this class of receptors is based in part on studies of bacteriorhodopsin, the detailed structure of which has been determined by crystallography). The intracellular (or cytoplasmic) domain of the receptor interacts with the interior of the cell or organelle, relaying the signal (~~www.wikipedia.com~~ website at wikipedia.com).

Please replace the paragraph on page 6, lines 8-15, with the following new paragraph:

Many transmembrane receptors are composed of two or more protein subunits which operate collectively and may dissociate when ligands bind, fall off, or at another stage of their "activation" cycles. They are often classified based on their molecular structure, or because the structure is unknown in any detail for all but a few receptors, based on their hypothesized (and sometimes experimentally verified) membrane topology. The polypeptide chains of the simplest are predicted to cross the lipid bilayer

only once, while others cross as many as seven times (the so-called G-protein coupled receptors) (~~www.wikipedia.com~~ website at wikipedia.com).